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Low free triiodothyronine levels in mexican pediatric population with congenital heart disease after cardiac surgery undergoing cardiopulmonary bypass.

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Abstract

BACKGROUND: Low free triiodothyronine level in patients undergoing heart surgery with cardiopulmonary bypass (CPB) is well described in literature, but the prevalence in pediatric Mexican population is yet unknown.

OBJECTIVE: To know the prevalence of postoperative low free triiodothyronine level and the associated complications after cardiopulmonary bypass exposure in pediatric population in Mexico.

MATERIAL AND METHODS: A sample of free triiodothyronine (FT3) blood was obtained in the early postoperative period of patients undergoing CPB heart surgery. *Postoperative low FT3 level (PLFT3) was defined as any blood value under 2.9 pg/mL.* Logistical regression models were used for analysis of independent variables, adjusted for complexity score (RACHS-1) and Aristotle Comprehensive Complexity Score.

RESULTS. *PLFT3* was present in 35.7% of the patients (n=109). Correlation with *PLFT3* the following variables were observed: prolonged CPB time (p=0.001) prolonged aortic cross clamp (p=0.002) level of complexity of the surgery as measured by Aristotle ≥3 (p=0.001) and RACHS-1 ≥3 (p=0.021). Associated complications were: postoperative arrhythmias (p=0.008) extended intubation period (p=0.008) and higher infection rate (p=0.002).

KEYWORDS: triiodothyronine; pediatric cardiac surgery, cardiopulmonary-bypass

BACKGROUND

Around 18,000 children in Mexico with a congenital heart disease *every year* are born. About 70% of them require a surgi-

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cal procedure during their first year of life. It is estimated that each year, almost 3,500 children under 5 years of age die from heart disease in our country.[1]

According to some reports, the *prevalence of PLFT3* in patients undergoing congenital heart surgery with cardiopulmonary bypass varies from 5 to 30%. Although *PLFT3* has not been related to a higher mortality, it has been associated with increased in-hospital length of stay (IH-LOS) and intensive care unit length of stay (ICU-LOS) increased use of inotropes, and duration of mechanical ventilation.[2-5]

Sick euthyroid syndrome, a state related to stress conditions as in shock, severe trauma, and different surgical procedures, has also been associated with the use of CPB in children and adults.[2,4,6-9]

Variables as age, nutritional status, CPB time, complexity of heart' malformation and the presence of associated genetic syndromes, have been found to be related with the development of PLFT3; its incidence in different series, varies from 10 to 30%.[6,7,9]

We report the *prevalence* of *PLFT3* after congenital heart surgery and CPB in our population.

OBJECTIVE

To know the prevalence of PLFT3 and the associated complications after CPB exposure in pediatric population in Mexico.

MATERIAL AND METHODS

A total of 109 consecutive children undergoing congenital heart surgery with CPB were included in the study.

Patients were classified according to the RACHS-1 score and Aristotle Comprehensive complexity score in order to categorize their surgical risk. Patients were classified in categories 1 to 6 of the RACHS-1 score and in groups I and V of the Aristotle Comprehensive Complexity Score.

Demographic data including geographical origin, weight, size, age, nutritional status, and associated condition were recorded.

Postoperative data included: ICU-LOS, IH-LOS, CPB duration, aortic cross clamp time initial, lactate levels at the intensive care unit and 24 h after surgery, duration of mechanical ventilation, postoperative morbidity: infection, bleeding, arrhythmias, low cardiac output and mortality.

A blood sample for the study was obtained along with the routine postoperative laboratory tests at patient's arrival to the cardiac intensive care unit. Specifically for FT3 determination, an Architect Ci8200 Analyzer (Abbott Diagnostic Industries TM, Illinois, USA) was used. *Postoperative low FT3 level (PLFT3) was defined as any FT3 blood value under 2. pg/mL.*

Statistical analysis

Data were analyzed using STATA Statistic software, vr. 12.0 (Stat Corp, Texas, USA).

Descriptive data such as population demographics and incidence of PLFT3 in different sub-groups, were expressed as proportions and means.

Levels of FT3 and risk categories (RACHS-1 and Aristotle Complexity Score) were dichotomized and Chi-square test was used for the analysis.

Continuous variables were reported as averages, using Mann Whitney test.

Logistical regression models were used for analysis of independent variables, which were

adjusted for age, gender and complexity score (RACHS-1).

A p-value < 0.05 was considered significant.

RESULTS

General demography is shown in **Table 1**. Mean value FT3 for the cohort was 3.03 ± 0.68 (PLFT3 T3L 2.33 ± 0.42 and No PLFT3 3.44 ± 0.44). PLFT3 were present in 39 patients (35.7%) with a higher incidence in children under one year (55.5%). In patients older than 10 years of age incidence observed was 52.6%. The incidence was also higher in patients with Down's syndrome (47.6%), which represented 19.2% of our population.

In our cohort comorbidities were present in 41.2%. In this population, *Postoperativelow free triiodothyronine level* was present in 42.2% (31.2% in patients without comorbidities).

The most frequent comorbidity in the cohort was malnutrition, with an associated *Postoperative low free triiodothyronine level* rate of 38.8%.

Variables significantly associated with *PLFT3* were: surgical complexity (RACHS-1 >3, p=0.018) Aristotle Complexity group 4 (p=0.004) aortic cross clamp time (p=0.001) and cardiopulmonary bypass time (p=< 0.001).

Patients with *PLFT3* were more likely to develop some type of complication (p=0.001) such as infections (p=0.019) and arrhythmias (p=0.001) Also, these patients and a longer ICU-LOS (p=0.065).

Patients with *PLFT3* were could not be extubated early (considering a 24 hourperiod) as compared with patients without *PLFT3* (p=0.003) **(Table 2)**. Logistic regression model for aortic cross clamp time showed an odds ratio (OR) of 1.023, meaning that for every extra minute of aortic cross clamp, there was a 2.3% higher probability for patients to develop *PLFT3*.

OR for CPB time was 1. 022, indicating that for every extra minute that a patient was under CPB, there was a 2.2% higher probability of developing *PLFT3* **(Table 3)**.

DISCUSSION

The best treatment for patients with congenital heart disease is dependent of highly specialized surgeons.

Table 1. Demographics

	Without PLFT3 N (%)	With PLFT3 N (%)
Number of patients (N 109)	70 (64.2%)	39 (35.7%)
Age (years)	5.5	5.5
Weight (kg)	18.6	18.8
Male	26 (63%)	15 (36%)
Female	44 (64%)	24 (35%)
Down's syndrome	11 (52%)	10 (47%)
Malnutrition	33 (61%)	21 (38%)
Disease (not related to the heart)	26 (57%)	19 (42%)

Table 2. Immediate postoperative results

	Without PLFT3 N (%)	With PLFT3 N (%)	P-Value
Bypass time (min)	82.6	133.2	<0.001[w]
Aortic cross clamp time (min)	46.4	83.7	0.001[w]
RACHS 3	3 (30%)	7 (70%)	0.018[c]
Higher surgical risk (≥ARIST. 3)	13 (39%)	20 (61%)	<0.001[c]
Extubation in the OR	52 (73%)	19 (27%)	0.007[c]
Early extubation (≤24 hours)	65 (68%)	30 (32%)	0.017[c]

[c]Chi square test. [w]Wilcoxon test (Mann- Whitney).

Table 3. Model of logistical regression

	OR	Wald	Sig	IC-95%	
Aortic cross clamp time	1.023*	19.5	<0.001	1.009	1.037
Cardiopulmonary bypass time	1.022*	21.9	<0.001	1.010	1.033

*Adjusted by age, sex and RACHS -1 score.

In low and mid income countries, this is still far from being achieved. However, some progress has taken place in early diagnosis, stabilization, and management of these patients.[10,11]

Congenital heart surgery has been highly perfected in the last decades, with an exceptional development in surgical techniques and intra and postoperative care, along with the creation of excellent intensive care units. All of this has significantly improved outcomes, not only decreasing mortality, but also improving the quality of life of survivors.

Continuous improvement in cardiopulmonary bypass techniques has been essential to in the performance of surgical procedures, and therefore to operate previously considered inoperable malformation;[10-12] however, some it complications are inevitable, mostly due to the exposure of blood to the plastic (non-endothelized) tubing used in CPB; to the shearing forces sustained by the blood and to some surgical techniques such as hypothermia and hypothermic circulatory arrest, which cause severe blood, tissue and other vital organs damage.

It is well known that cardiopulmonary bypass induces cardio-depressor changes, and pro-inflammatory and immunosuppressive responses, as well as some degree of vasomotor disorder and hormonal disorders, all of which can impact in a negative way on the myocardium and other organs and systems.[3,4,9]

The aforementioned disruptions are more evident when prolonged aortic cross clamp (>60 minutes) and CPB time (>90′) periods are associated.[3,4,5-7,9]

Thyroid hormones have a key role in the normal function of the heart. They have a direct effect when used in their free active form, or an indirect participation through favored or suppressed mechanisms induced by them.

On the other hand, they also have direct influence on the regulation of heart rate and rhythm, myocardial contraction and regulation of coronary blood flow. Likewise, they participate in the regulation of vasomotor tone, promoting vasodilation in the peripheral and pulmonary systems. Their effect on the cardiovascular system depends on genetic and non-genetic factors and they involve the modification of the expression of beta-receptors in myocardium, the stimulation of proteins associated to calcium such as SERCA (sarcoplasmic reticulum calcium ATPase) and the inhibition of its counter-regulatory hormone fosfolambam.[6,7,8]

Their effects in blood vessels, seem to be due to the release of other vasodilator substances, within the endothelium, in response to the increase of metabolic rate and oxygen consumption. Simultaneously, there is a direct effect of the hormone on the pulmonary vasculature, which induces an after load reduction, and at the same time, an increase in preload by increasing venous return, with a positive effect on cardiac output and systemic perfusion. The excess and the deficit of thyroid hormones determine pathological states clinically well defined.[6-9,13]

Derangement in all thyroid hormones levels (including thyroid stimulating hormone) has been described elsewhere; however, changes in T3 and specially in free T3 levels are probably

the most important, not only for their clinical relevance, but also due to the fact that their reduction have been documented early and in a constant pattern in previous studies.[4,6,9,13-15]

Postoperative low levels of T3 and FT3 have been related to adverse postoperative outcomes, with significant increases in IH-LOS, use of inotropic drugs and mechanical ventilatory support requirements in every type of cardiac surgery with CBP.[5-7,13-15]

Higher RACHS-1 and Aristotle classification, arrhythmias *rate*, longer ICU-LOS and duration of mechanical ventilation were also found to be related to *PLFT3*. *PLFT3* was also found in patients under one year and in those over ten years of age, and in patients with Down's syndrome (50% of patients with Down's syndrome had *PLFT3*). Our results coincide with those reported in the literature.[4,5,7-9,15]

Actually different protocols have been developed to treat PLFT3, all of which have shown an improvement of the levels and the affected variables. However, due to the high cost of intravenous treatment, research is still going on to find the best way to deliver the hormone.[16-18]

In conclusion, in our population the *prevalence* of *PLFT3* in children undergoing congenital heart surgery with CPB, is slightly more frequent than the one informed elsewhere.

Different factors, including cardiopulmonary bypass time, aortic cross clamp time, Down's syndrome, poor nutrition status and age are associated. Based on our results, we believe that complete screening for preoperative and postoperative Thyroid hormone function, should be routinely done in all the patients to will need cardiac surgery with cardiopulmonary bypass.

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